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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/565,048	01/17/2006	Kristen E. Belmonte	PU60399	3931

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EXAMINER	
GALLIS, DAVID E	

ART UNIT	PAPER NUMBER
1625	

NOTIFICATION DATE	DELIVERY MODE
12/07/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

US_cipkop@gsk.com

Office Action Summary	Application No.	Applicant(s)	
	10/565,048	BELMONTE ET AL.	
	Examiner	Art Unit	
	David E. Gallis	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) *1-5* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/17/06 and 11/20/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1 through 13 are pending. Claims 2 through 4 have been withdrawn. Applicants' claim to priority from provisional application 60/487982, filed July 7, 2003 is acknowledged.

Election/Restrictions

2. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1 through 5, drawn to a compound of Formula (I) and a pharmaceutical composition comprising Formula (I), classified in class 546, and subclass 125.

II. Claims 6 through 13, and claim 1 (in part) drawn to methods of inhibiting the binding of acetylcholine to its receptors using a compound of formula (I), treating muscarinic acetylcholine receptor mediated diseases using a compound of formula (I), and administration of a compound of formula (I), classified in class 514, and subclass 304.

3. Inventions I and II are related as product and methods of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product. See MPEP § 806.05(h). In the instant case there are other treatments for affecting muscarinic acetylcholine receptor mediated diseases. For example, metaproterenol and albuterol are used effectively in the treatment of asthma.

4. Invention Group II was elected without traverse by applicants' representative, Dara Dinner, by telephone on the morning of November 19, 2007. The examiner has withdrawn non-elected claims 1 through 5. This restriction is hereby MADE FINAL.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 5 through 13 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

7. Claim 6 is drawn to method of inhibiting the binding of acetylcholine to its receptors comprising administering a safe and effective amount of a compound of formula (I). Claim 7 is drawn to a method of treating a muscarinic acetylcholine receptor mediated disease comprising administering safe and effective amount of a compound of formula (I). Claims 8 and 9 further limit claim 7 to the treatment of a selected list of diseases, and administration via inhalation via nose or mouth. Claim 10 again further limits administration via reservoir drypowder, multi-dose dry powder, or metered dose inhalers. Claims 11, 12, and 13 further limit claim 7 to 1 mg dosages with 12, 24, and 36 hour or longer durations of action respectively.

8. While the disclosure references some chemically anti-cholinergic compounds and methods of analysis of formula (I) compounds, there is no data disclosed to enable the compounds' usage for the methods claimed. The disclosure outlines the analysis of inhibition of receptor action, muscarinic receptor binding assays, evaluation of potentcy and duration of action, induced bronchoconstriction potency and duration of action, and formulation and administration. In several instances the disclosure reports plotting and analyzing data, generating concentration response curves, and determining duration of activity, however, the disclosure is devoid of any data that would enable one skilled in the art to use the invention, and especially in a "safe and effective" manner. With the lack of disclosed data, there is no evidence disclosed that suggests that the compounds of formula (I) have any therapeutic activity at all toward the muscarinic acetylcholine receptor mediation, acetylcholine binding inhibition, and the diseases of claim 8. Furthermore, there is no formulation data to support the durations of action of claims 11 through 13 based on 1 mg dosages.

"The factors to be considered [in making an enablement rejection] have been summarized as a) the quantity of experimentation necessary, b) the amount of direction or guidance presented, c) the presence or absence of working examples, d) the nature of the invention, e) the state of the prior art, f) the relative skill of those in that art, g) the predictability or unpredictability of the art, h) and the breadth of the claims", In re Rainer, 146 USPQ 218 (1965); In re Colianni, 195 USPQ 150, Ex parte Formal, 230 USPQ 546. a) Determining the "safe and effective" amounts of a compound of formula (I) would require extensive experimentation. b) The direction concerning the analysis of inhibition

of receptor action, muscarinic receptor binding assays, evaluation of potentcy and duration of action, induced bronchoconstriction potency and duration of action are found throughout the disclosure on pages 5 through 9. c) There is no working example of a effectiveness of a compound of formula (I). d) The nature of the invention is biochemical. e) The state of the chemical art currently lacks knowledge of the general effectivness of a formula (I) compound for the methods claimed. f) Artisans using Applicant's invention would require a Ph.D. degree, and possibly an MD, and several years of research experience. g) It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved", and receptor inhibition is generally considered to be an unpredictable factor. See In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). h) The breadth of the claims includes methods of receptor inhibition and disease treatments requiring experimental data not available in the disclosure.

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 6 and 7 depend from non-elected claim 1. There is insufficient antecedent basis for this dependency since claim 1 has been withdrawn. Claims 6 and 7 require the incorporation of Formula (I) in order to overcome this rejection.

11. Claims 8 through 13 are rejected due to their dependency on claim 7.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David E. Gallis whose telephone number is 571-272-9068. The examiner can normally be reached on Mon-Thur 8:30-7:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on 571-272-1600. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

David E. Gallis
Patent Examiner

BERNARD DENTZ
PRIMARY EXAMINER